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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,583	05/23/2006	David Borsook	04843/144002	4263

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EXAMINER	
BOR, HELENE CATHERINE	
ART UNIT	PAPER NUMBER
3768	
MAIL DATE	DELIVERY MODE
08/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,583	BORSOOK ET AL.	
	Examiner	Art Unit	
	Helene Bor	3768	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: Journal Article

DETAILED ACTION

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because:
> It does not identify the city and either state or foreign country of residence of each inventor. The residence information may be provided on either an application data sheet or supplemental oath or declaration.
>
> It does not identify the mailing address of each inventor. A mailing address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing address should include the ZIP Code designation. The mailing address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claim 1-5, 9-11, 14-15 & 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Beccerra'563 et al. (US Patent No. 2002/0042563 A1).

Claim 1: Beccerra'563 teaches a method for identifying a target for analgesic therapy, said method comprising the steps of: (a) providing a first and a second non-human subject, wherein said subjects have a genetic-based difference in nociception (Page 14, Para 0179); (b) performing an fMRI on the brain of said first subject during or following administration of a painful stimulus; (c) performing an fMRI on the brain of said second subject during or following administration of said painful stimulus (Page 31, Para 0358 & Page 38, Para 0458); and (d) comparing the results of said fMRI on the brain of said first subject with the results of said fMRI on the brain of said second subject to identify a brain region that is differentially activated in response to said painful stimulus, said brain region being a target for analgesic therapy (Page 14, Para 0179, Page 39, Para 0462 – 0464).

Claim 2/1: Beccerra'563 teaches a method, wherein said method further comprises the steps of: (e) administering an analgesic; (f) performing a second fMRI on the brain of said first subject during or following a second administration of said painful stimulus; (g) performing a second fMRI on the brain of said second subject during or following a second administration of said painful stimulus; and (h) comparing the results of said second fMRIs to identify a brain region that is differentially activated in response to said painful stimulus in the presence of said analgesic, said brain region being a target for analgesic therapy (Page 14, Para 0178, Page 38, Para 0459 & Page 39, Para 0462 –

0464 & 0469).

Claim 3/1: Beccerra'563 teaches a method, wherein, prior to, simultaneous with, or following administration of said painful stimulus, an analgesic is administered to said first subject and said second subject and, in step (d), said brain region is differentially activated in response to said painful stimulus, said analgesic, or both (Page 25, Para 0298 & Page 38, Para 0458).

Claim 4/1: Beccerra'563 teaches a method, wherein said method further comprises the step of: (e) assessing gene expression in said target brain region identified in step (d) to further identify a gene or gene product that is differentially expressed, wherein said differentially expressed gene or gene product is a target for analgesic therapy (Page 38, Para 0458 & Page 39, Para 0465 & 0469).

Claim 5/2/1: Beccerra'563 teaches a method, wherein said method further comprises the step of: (i) assessing gene expression in said target brain region identified in step (h) to further identify a gene or gene product that is differentially expressed, wherein said differentially expressed gene or gene product is a target for analgesic therapy (Page 38, Para 0459 & Page 39, Para 0464, 0465 & 0469).

Claim 9/1, 10/1, & 11/10/1: Beccerra'563 teaches a method, wherein said painful stimulus is an acute pain stimulus. Beccerra'563 teaches a method, wherein said painful stimulus is a chronic pain stimulus. Beccerra'563 teaches a method, wherein said chronic pain stimulus is neuropathic pain, arthritic pain, or cancer pain (Page 25, Para 0296).

Claim 14: Beccerra'563 teaches a method for identifying a target for analgesic therapy,

said method comprising the steps of: (a) administering an analgesic to a first and a second non-human subject, wherein said subjects have a genetic-based difference in nociception; (b) performing a first fMRI on the brain of said first subject during or following administration of said analgesic; (c) performing a first fMRI on the brain of said second subject during or following administration of said analgesic; and (d) comparing the results of said fMRI on the brain of said first subject with the results of said fMRI on the brain of said second subject to identify a brain region that is differentially activated in response to said analgesic administration, said brain region being a target for analgesic therapy. (As discussed in Claim 1 & 2)

Claim 15/14: Beccerra'563 teaches a method, wherein said method further comprises the step of: (e) assessing gene expression in said target brain region identified in step (d) to further identify a gene or gene product that is differentially expressed, wherein said differentially expressed gene or gene product is a target for analgesic therapy (Page 1, Para 0004, Page 19, Para 0232, Page 25, Para 0295 & Claim 23).

Claim 21/14: Beccerra'563 teaches a method, wherein said analgesic is morphine (Page 15, Para 0192).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claim 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beccerra'563 et al. (US Patent No. 2002/0042563 A1) and further in view of Jeffrey S. Mogil et al. (Jeffery S. Mogil and Seetal M. Adhikari. Hot and Cold Nociception Are Genetically Correlated. The Journal of Neuroscience, 1999. Vol. 19, Pages 1-5.)

Claim 6/1: Beccerra'563 teaches using animals as subjects (Page 14, Para 0179). Beccerra'563 does not specifically mention wherein said first subject and said second subject are rodents. However, Mogil teaches the subjects to be mice or rodents (abstract). Thus, it would have been obvious to a person of ordinary skill in the art to try the mice of Mogil's experiment as the test subjects of Beccera'563 as a person with ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. One of ordinary skill would try known options such as pigs, monkeys, apes, rats, mice, humans or other known test subjects to complete the experiment.

Claim 7/6 & 8/6: Beccerra'563 teaches using animals as subjects (Page 14, Para 0179) and teaches the experiment being adapted for testing gene products or therapies

(Page 1, Para 0004, Page 19, Para 0232, Page 25, Para 0295 & Claim 23). Beccerra'563 does not specifically mention wherein said first subject and said second subject are rodents with of different strains such as 129P3, A, AKR, BALB/c, C3H/He, C57BL/6, C57BL/10, C58, CBA, DBA/2, RIIIS, SM, LP, SJL, and SWR. However, Mogil teaches the subjects to be mice or rodents with different strains (abstract). Since both Mogil and Beccerra'563 teach the use of gene therapy, the combination of the two would have been obvious because the design incentive provides a reason to make the adaptation. Also due to the application of the prior knowledge, the invention resulted in a predictable manner. In experiments involving genes such as Mogil and Beccerra'563 the use of mice with different known strains as test subjects is desired as to improve the accuracy of the experiment and limit variabilities.

Claim 16/14, 26/22, 36/32, 43/42 & 50/48: Beccerra'563 teaches using animals as subjects (Page 14, Para 0179). Beccerra'563 does not specifically mention wherein said first subject and said second subject are rodents. However, Mogil teaches the subjects to be mice or rodents (abstract). Thus, it would have been obvious to a person of ordinary skill in the art to try the mice of Mogil's experiment as the test subjects of Beccera'563 as a person with ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. One of ordinary skill would try known options such as pigs, monkeys, apes, rats, mice, humans or other known test subjects to complete the experiment.

Claim 17/16 & 18/16: Beccerra'563 teaches using animals as subjects (Page 14, Para

0179) and teaches the experiment being adapted for testing gene products or therapies (Page 1, Para 0004, Page 19, Para 0232, Page 25, Para 0295 & Claim 23). Beccerra'563 does not specifically mention wherein said first subject and said second subject are rodents with of different strains such as 129P3, A, AKR, BALB/c, C3H/He, C57BL/6, C57BL/10, C58, CBA, DBA/2, RIIIS, SM, LP, SJL, and SWR. However, Mogil teaches the subjects to be mice or rodents with different strains (abstract). Since both Mogil and Beccerra'563 teach the use of gene therapy, the combination of the two would have been obvious because the design incentive provides a reason to make the adaptation. Also due to the application of the prior knowledge, the invention resulted in a predictable manner. In experiments involving genes such as Mogil and Beccerra'563 the use of mice with different known strains as test subjects is desired as to improve the accuracy of the experiment and limit variabilities.

Claim 12/1: Beccerra'563 teaches, wherein said painful stimulus is a stimulus that induces a hypersensitive response (Page 39, Para 0465). Beccerra'563 teaches testing drugs, which has desirable effects. It would have been obvious to one of ordinary skill in the art that a desirable effects for testing would be a hypersensitive response especially when evaluating drugs (Page 39, Para 0465).

Claim 30/22, 40/32: Beccerra'563 teaches, wherein said painful stimulus is a stimulus that induces a hypersensitive response (Page 39, Para 0465). Beccerra'563 teaches testing drugs, which has desirable effects. It would have been obvious to one of ordinary skill in the art that a desirable effects for testing would be a hypersensitive response especially when evaluating drugs (Page 39, Para 0465).

Claim 13/1: Beccerra'563 teaches, wherein said first subject and said second subject are conscious (Page 37, Para 0438). Beccera'563 doesn't specifically teach the subjects being conscious. However, it is obvious to one of ordinary skill in the art that the subject were conscious to provide feedback to the VAs scale.

Claim 19/14, 31/22, 41/32, 47/42, 54/48: Beccerra'563 teaches, wherein said painful stimulus is a stimulus that induces a hypersensitive response (Page 39, Para 0465). Beccerra'563 teaches testing drugs, which has desirable effects. It would have been obvious to one of ordinary skill in the art that a desirable effects for testing would be a hypersensitive response especially when evaluating drugs (Page 39, Para 0465).

Claim 20/14: Beccerra'563 teaches, wherein said analgesic is a channel blocker, antidepressant, μ-opioid receptor agonist, κ-opioid receptor agonist, cannabinoid receptor agonist, nicotinic receptor agonist, or adrenergic receptor agonist (Page 8, Para 0129).

Claim 44/42, 51/48: Beccerra'563 teaches, wherein said analgesic is a channel blocker, antidepressant, μ-opioid receptor agonist, κ-opioid receptor agonist, cannabinoid receptor agonist, nicotinic receptor agonist, or adrenergic receptor agonist (Page 8, Para 0129).

Claim 22: Beccerra'563 teaches a method for identifying a target for analgesic therapy, said method comprising the steps of: (a) providing a first and a second non-human subject, wherein said subjects have a genetic-based difference in nociception (Page 14, Para 0179); (b) performing an fMRI on the brain of said first subject during or following administration of a painful stimulus; (c) performing an fMRI on the brain of said second

subject during or following administration of said painful stimulus (Page 31, Para 0358 & Page 38, Para 0458); and (d) comparing the results of said fMRI on the brain of said first subject with the results of said fMRI on the brain of said second subject to identify a brain region that is differentially activated in response to said painful stimulus, said brain region being a target for analgesic therapy (Page 14, Para 0179, Page 39, Para 0462 – 0464). Beccerra'563 teaches a method, wherein said method further comprises the steps of: (e) administering an analgesic; (f) performing a second fMRI on the brain of said first subject during or following a second administration of said painful stimulus; (g) performing a second fMRI on the brain of said second subject during or following a second administration of said painful stimulus; and (h) comparing the results of said second fMRIs to identify a brain region that is differentially activated in response to said painful stimulus in the presence of said analgesic, said brain region being a target for analgesic therapy (Page 14, Para 0178, Page 38, Para 0459 & Page 39, Para 0462 – 0464 & 0469). Beccerra'563 teaches a method for determining the efficacy of a gene or gene product. Beccerra'563 doesn't teach the subject having certain genes. However, Mogil teaches providing a first and a second non-human subject, said second non-human subject differing from said first non-human subject in its expression of a transgene of interest (Figure 1). It would have been obvious to one of ordinary skill in the art to combine the teachings of Beccerra'563 and Mogil in order for understanding genetic correlations among traits (Page 1 right column).

Claim 23/22: Beccerra'563 teaches a method, wherein said method further comprises the steps of: (e) administering an analgesic; (f) performing a second fMRI on the brain

of said first subject during or following a second administration of said painful stimulus; (g) performing a second fMRI on the brain of said second subject during or following a second administration of said painful stimulus; and (h) comparing the results of said second fMRIs to identify a brain region that is differentially activated in response to said painful stimulus in the presence of said analgesic, said brain region being a target for analgesic therapy (Page 14, Para 0178, Page 38, Para 0459 & Page 39, Para 0462 – 0464 & 0469).

Claim 24/22, 34/32: Beccerra'563 teaches a method, wherein, prior to, simultaneous with, or following administration of said painful stimulus, an analgesic is administered to said first subject and said second subject and, in step (d), said brain region is differentially activated in response to said painful stimulus, said analgesic, or both (Page 25, Para 0298 & Page 38, Para 0458).

Claim 25/22: Beccerra'563 teaches a method for identifying a target for analgesic therapy, said method comprising the steps of: (a) providing a first and a second non-human subject, wherein said subjects have a genetic-based difference in nociception (Page 14, Para 0179); (b) performing an fMRI on the brain of said first subject during or following administration of a painful stimulus; (c) performing an fMRI on the brain of said second subject during or following administration of said painful stimulus (Page 31, Para 0358 & Page 38, Para 0458); and (d) comparing the results of said fMRI on the brain of said first subject with the results of said fMRI on the brain of said second subject to identify a brain region that is differentially activated in response to said painful stimulus, said brain region being a target for analgesic therapy (Page 14, Para 0179, Page 39,

Para 0462 – 0464). Beccerra'563 teaches a method, wherein said method further comprises the steps of: (e) administering an analgesic; (f) performing a second fMRI on the brain of said first subject during or following a second administration of said painful stimulus; (g) performing a second fMRI on the brain of said second subject during or following a second administration of said painful stimulus; and (h) comparing the results of said second fMRIs to identify a brain region that is differentially activated in response to said painful stimulus in the presence of said analgesic, said brain region being a target for analgesic therapy (Page 14, Para 0178, Page 38, Para 0459 & Page 39, Para 0462 – 0464 & 0469). Beccerra'563 teaches a method for determining the efficacy of a gene or gene product. Beccerra'563 doesn't teach the subject having certain genes. However, Mogil teaches providing a first and a second non-human subject, said second non-human subject differing from said first non-human subject in its expression of a transgene of interest (Figure 1). It would have been obvious to one of ordinary skill in the art to combine the teachings of Beccerra'563 and Mogil in order for understanding genetic correlations among traits (Page 1 right column). Beccerra'563 teaches the method focusing on the central nervous system (Claim 31).

Claim 32, 33/32, 35/32, 42, 48 & 49/48: Beccerra'563 teaches a method for identifying a target for analgesic therapy, said method comprising the steps of: (a) providing a first and a second non-human subject, wherein said subjects have a genetic-based difference in nociception (Page 14, Para 0179); (b) performing an fMRI on the brain of said first subject during or following administration of a painful stimulus; (c) performing an fMRI on the brain of said second subject during or following administration of said

painful stimulus (Page 31, Para 0358 & Page 38, Para 0458); and (d) comparing the results of said fMRI on the brain of said first subject with the results of said fMRI on the brain of said second subject to identify a brain region that is differentially activated in response to said painful stimulus, said brain region being a target for analgesic therapy (Page 14, Para 0179, Page 39, Para 0462 – 0464). Beccerra'563 teaches a method, wherein said method further comprises the steps of: (e) administering an analgesic; (f) performing a second fMRI on the brain of said first subject during or following a second administration of said painful stimulus; (g) performing a second fMRI on the brain of said second subject during or following a second administration of said painful stimulus; and (h) comparing the results of said second fMRIs to identify a brain region that is differentially activated in response to said painful stimulus in the presence of said analgesic, said brain region being a target for analgesic therapy (Page 14, Para 0178, Page 38, Para 0459 & Page 39, Para 0462 – 0464 & 0469). Beccerra'563 teaches a method for determining the efficacy of a gene or gene product. Beccerra'563 doesn't teach the subject having certain genes. However, Mogil teaches providing a first and a second non-human subject, said second non-human subject differing from said first non-human subject in its expression of a transgene of interest (Figure 1). It would have been obvious to one of ordinary skill in the art to combine the teachings of Beccerra'563 and Mogil in order for understanding genetic correlations among traits (Page 1 right column).

Claim 27/22, 28/22, 29/28/22: Beccerra'563 teaches a method, wherein said painful stimulus is an acute pain stimulus. Beccerra'563 teaches a method, wherein said

painful stimulus is a chronic pain stimulus. Beccerra'563 teaches a method, wherein said chronic pain stimulus is neuropathic pain, arthritic pain, or cancer pain (Page 25, Para 0296).

Claim 46/42 & 53/48: Beccerra'563 teaches a method, wherein, prior to step (a), said first and said second non-human subjects are administered a painful stimulus (Page 39, Para 0468).

Claim 45/42, 52/48: Beccerra'563 teaches a method, wherein said analgesic is morphine (Page 15, Para 0192).

Claim 37/32, 38/32, 39/38/32: Beccerra'563 teaches a method, wherein said painful stimulus is an acute pain stimulus. Beccerra'563 teaches a method, wherein said painful stimulus is a chronic pain stimulus. Beccerra'563 teaches a method, wherein said chronic pain stimulus is neuropathic pain, arthritic pain, or cancer pain (Page 25, Para 0296).

Conclusion

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

a. Breiter, Hans et al. Drug development by rapid neuroimaging of neural cells, 11/13/2003, US 20030211459 A1.

b. England; Robert L. Objective determination of chronic pain in patients, 04/27/2006. US 20060089551 A1.

c. Mueller; Edgar. Method for time-resolved and location-resolved presentation of functional brain activities with magnetic resonance and apparatus for the implementation of the method, 09/11/2001. US 6289234 B1.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Helene Bor whose telephone number is 571-272-2947. The examiner can normally be reached on M-F 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eleni Mantis-Mercader can be reached on 571-272-4740. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

hcb

ELENI MANTIS MERCADER
SUPERVISORY PATENT EXAMINER

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